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54) Title: TRANSPARENT COMPOSITION  57) Abstract  A transparent composition comprising a phospholipid carrier. The concentration of the water-soluble nonionic p	, a wate	r-soluble nonionic polymer, an oily component, and a cosmetic acceptable in the composition is less than 2.0 wt% by weight of the composition.

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WO 00/61098 PCT/US99/08232

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### TRANSPARENT COMPOSITION

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### **FIELD**

The present invention relates to a transparent composition. In particular, it relates to a transparent composition for moisturizing the skin.

### **BACKGROUND**

Many personal care products currently available to consumers are directed primarily to improving the health and/or physical appearance of the skin. Among these skin care products, many are directed to delaying, minimizing or even eliminating histological changes of skin typically associated with skin aging or environmental damage to human skin. In order to maintain or return skin to a healthy and/or youthful state, the skin is typically treated with a moisturizing agent. Known moisturizing agents include various oily components and humectants, e.g., glycol or glycerin. Generally, the higher the concentration of such agents, the more the moisturization effect to the skin.

However, increasing the level of such agents, particularly raising the concentration of oily components used in emulsions, tends to impart greasy feeling of skin and may feel sticky. However, the reduction of such oily components may result in poor distribution/spreading of the moisturizing agent. In addition, surfactants in formulations may sometimes cause sticky and tacky feeling of the skin.

Phospholipids are known in cosmetics and/or pharmaceuticals, as ingredients which provide moisture retaining of skin. Such phospholipids includes ingredients derived from natural sources and synthetic ingredients. Recently, phospholipids has been useful in various formulation, particularly in emulsion (aqueous composition), due to the structural properties as emulsifying agents and/or solubilizing agents. But phospholipid containing compositions that feel less greasy on the consumer's skin may be unacceptable to consumers

because they are less spreadable and do not feel as "rich" when applied to the skin. In addition, due to their property as emulsifying agents, the phospholipids are commonly used in compositions that are not transparent.

Based on the foregoing, there is a need for a transparent composition for improving one's skin condition by maximizing the amount of moisturizing agent, improving the spreadability of the composition to the skin, yet continues to impart a non-greasy feeling to the user.

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#### SUMMARY

The present invention is directed to a transparent composition comprising a phospholipid, a water-soluble nonionic polymer, an oily component, and a cosmetically-acceptable carrier, wherein the concentration of the water-soluble nonionic polymer is less than 2.0% by weight of the composition.

The transparent compositions containing the specified ingredients are useful for topical application and for providing improved transparency and spreadability of products and good skin feel such as moisturizing the skin without greasy feeling to skin. In addition, the composition of the present invention is stable in storage even at high temperature (about 40 degC).

These and other features, aspects, and advantages of the present invention will become better understood from a reading of the following description, and appended claims.

#### **DETAILED DESCRIPTION**

While the specification concludes with claims particularly pointing out and distinctly claiming the invention, it is believed that the present invention will be better understood from the following description.

All percentages, ratios, and levels of ingredients referred to herein are based on the actually total amount of the composition, unless otherwise indicated.

All measurements referred to herein are made at 25°C unless otherwise specified.

All publications, patent applications, and issued patents mentioned herein are hereby incorporated in their entirety by reference. Citation of any reference is not an admission regarding any determination as to its availability as prior art to the claimed invention.

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Herein, "comprising" means that other steps and other ingredients which do not affect the end result can be added. This term encompasses the terms "consisting of" and "consisting essentially of."

Herein, "topical application" means to apply or spread a material onto the surface of the skin.

Herein, "cosmetically-acceptable carrier," means one or more compatible dermatologically-acceptable solid or liquid filler diluents or encapsulating substances.

Herein, "dermatologically-acceptable," means that the compositions or components thereof so described are suitable for use in contact with human skin without undue toxicity, incompatibility, instability, irritation allergic response, and the like, commensurate with a reasonable benefit/risk ratio.

Herein, "safe and effective amount," means an amount of a compound or composition sufficient to significantly induce a positive benefit, preferably a positive skin appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, *i.e.*, to provide a reasonable benefit to risk ratio, within the scope of sound judgment of the skilled artisan.

Herein, "mixtures" is meant to include a simple combination of materials and any compounds that may result from their combination.

All ingredients such as actives and other ingredients useful herein may be categorized or described by their cosmetic and/or therapeutic benefit or their postulated mode of action. However, it is to be understood that the active and other ingredients useful herein can, in some instances, provide more than one cosmetic and/or therapeutic benefit or operate via more than one mode of action. Therefore, classifications herein are made for the sake of convenience and are not intended to limit an ingredient to the particularly stated application or applications listed.

### A. Transparent Composition

The present invention is directed to a transparent composition comprising a phospholipid, a water-soluble nonionic polymer, an oily component, and a cosmetically-acceptable carrier. Herein, "transparent composition," means that the composition has transparency sufficient to see the other side when the composition is in a clear glass or plastic bottle which has about 1cm of diameter.

The transparent composition of the present invention has an apparent viscosity of from about 2 to about 10,000 centipoise (cps), preferably from about 3 to about 500 cps of viscosity, more preferably from about 4 to about 200 cps.

Such viscosity can be determined using a CJV 5000 Viscometer (AND, Tokyo, Japan). The viscosity is determined on the composition after the composition has been allowed to stabilize following its preparation, generally at least 24 hours under conditions of 25°C +/- 1°C and ambient pressure after preparation of the composition. Viscosity is measured with the composition at a temperature of 25°C +/- 1°C.

#### B. Phospholipids 10

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The transparent composition of the present invention contains a phospholipid component. Without being bound by the theory, it is believed that the phospholipid, generally known as amphiphilic surfactant derived from natural sources, tends to emulsify and/or solubilize a composition with water and/or oils. due to being an amphiphilic component.

Nonlimiting examples of phospholipids useful herein includes synthetic phospholipids such dialloylphosphatidylcholine and as dipalmitoyl phosphatidylcholine. phosphatidylcholine, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, and sphingomyelin; natural phospholipds include egg yolk lecithin and soybean lecithin extracted from egg yolk and soybean.

Preferably, the phospholipid used herein is lecithin. More specifically, "Lecithin" is 1,2-diacyl-sn-glycero-3-phosphocholone and derivatives thereof. which does not mean a "lecithin" as a group which are commercially and industrially available phospholipids.

The phospholipid component is present in the composition from about from about 0.05% to about 5.0%, preferably from about 0.1% to about 1.0%.

### Water-soluble Nonionic Polymer

The transparent composition of the present invention contains a watersoluble nonionic polymer. The water-soluble nonionic polymer herein is primarily a thickening agent. Without intending to be limited by theory, it is believed that anionic or cationic water-soluble polymers tend to interact with the phospholipids of this invention, resulting in an emulsion. Consequently, the emulsified composition is no longer transparent.

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In one embodiment, the water-soluble polymer described below can be provided in the form of both solid and liquid. The liquid form of the polymer may be provided in a water solution. The water solution is also transparent.

The concentration of the water-soluble nonionic polymer is less than 2.0% by weight of the composition, preferably from about 0.01% to about 2.0 %.

Water-soluble nonionic polymers useful herein include polysaccharides, gums, polyacrylamide, and mixtures thereof. Extract materials which are derived from natural sources (e.g., locust bean gum) can be included as water-soluble polymeric thickening agent. Locust bean gum is available from Pentapharm Ltd, (Basel, Switzerland).

(i) Polysaccharides: A wide variety of polysaccharides can be used in the present composition. Herein, "polysaccharides" refers to water-soluble nonionic polymers containing a backbone of a repeating mono saccharide (i.e., carbohydrate) units. Examples of polysaccharides include those selected from the group consisting of cellulose, hydroxyethylcellulose, hydroxyethyl ethylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, methyl hydroxyethylcellulose, and mixtures thereof. Also useful herein are the alkyl substituted celluloses. In these polymers, the hydroxy groups of the cellulose polymer is hydroxyalkylated (preferably hydroxyethylated or hydroxypropylated) to form a hydroxyalkylated cellulose which is then further modified with a C<sub>10-30</sub> straight chain or branched chain alkyl group through an ether linkage. Typically these polymers are ethers of C<sub>10-30</sub> straight or branched chain alcohols with hydroxyalkylcelluloses. Examples of alkyl groups useful herein include those selected from the group consisting of stearyl, isostearyl, lauryl, myristyl, cetyl, isocetyl, cocoyl (i.e., alkyl groups derived from the alcohols of coconut oil). palmityl, oleyl, linoleyl, linolenyl, ricinoleyl, behenyl, and mixtures thereof. Preferred water-soluble nonionic polymers are hydroxyethylcellulose and cetyl hydroxyethylcellulose.

(ii) Gums: Gums useful herein include materials which are primarily derived from natural sources. Examples of these gums include materials selected from the group consisting of amylopectin, amylose, dextrin, guar gum, hydroxypropyl guar, konjac mannan, locust bean gum, pullulan, sclerotium gum, tamarind seed gum, and mixtures thereof; preferably locust bean gum, pullulan, sclerotium gum, and termarind seed gum. Purified gums are preferable.

(iii) Polyacrylamide Polymers: Polyacrylamide polymers are also useful. Such nonionic polyacrylamide polymers include substituted branched or unbranched polymers. These polymers can be formed from a variety of monomers including acrylamide and methacrylamide which are unsubstituted or substituted with one or two alkyl groups (preferably C<sub>1-5</sub>). Preferred are acrylate amide and methacrylate amide monomers in which the amide nitrogen is unsubstituted, or substituted with one or two C<sub>1-5</sub> alkyl groups (preferably methyl, ethyl, or propyl), for example, acrylamide, methacrylamide, Nmethacrylamide, N-methylmethacrylamide, N,N-dimethylmethacrylamide, Nisopropylacrylamide, N-isopropylmethacrylamide, and N,N-dimethylacrylamide.

(iv) Crosslinked poly(N-vinylpyrrolidones): Crosslinked vinylpyrrolidones) useful herein include those described in US Patent No. 5,139,770, Shih et al. issued August 18, 1992, and US Patent No. 5,073,614, Shih et al. issued December 17, 1991, both patents of which are incorporated by reference herein in their entirety. Such crosslinked poly(N-vinylpyrrolidones) typically contain from about 0.25% to about 1% by weight of a crosslinking agent selected from the group consisting of divinyl ethers and diallyl ethers of terminal diols containing from about 2 to about 12 carbon atoms, divinyl ethers and diallyl ethers of polyethylene glycols containing from about 2 to about 600 units, dienes having from about 6 to about 20 carbon atoms, divinyl benzene, vinyl and allyl ethers of pentaerythritol, and the like. Typically, these gelling agents have a viscosity from about 25,000 cps to about 40,000 cps when measured as a 5% aqueous solution at 25°C using a Brookfield RVT viscometer with Spindle #6 at 10 rpm. Commercially available examples of these polymers include ACP-1120, ACP-1179, and ACP-1180, available from International Specialty Products (Wayne, NJ).

(v) Other Polymer: Additional water-soluble nonionic polymers which are suitable herein. include polyvinylalcohol. polyvinylpyrrolidones, polyvinylcaprolactam, and polyvinylformamide.

#### 30 Oily Component

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The transparent composition of the present invention contains an oily component. The oily component is used as an emollient. The oily component is present in the composition from about 0.05% to about 15.0%, preferably from about 0.1% to about 8.0%. Particularly, the level of the oily component depends on the desired form of the composition, such as a lotion or a gel. For example, if

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a composition with high viscosity is desired, the concentration of the oily component may be higher than in a low viscosity composition. Preferably, low viscosity compositions (e.g., lotion) contain from about 0.1% to about 2.0wt% of the oily component. High viscosity compositions (e.g., gel) contains from about 1.0% to about 8.0 wt% of the oily component.

A wide variety of suitable oil compounds are known and may be used herein and numerous examples can be found in <u>Sagarin</u>. <u>Cosmetics</u>, <u>Science</u> and <u>Technology</u>. <u>2nd Edition</u>, <u>Vol. 1</u>, <u>pp. 32-43 (1972)</u>. Preferably, the oily component is a mixture of two or more of the oily components described below. Nonlimiting examples of suitable oily components include:

(i) Mineral oil: Mineral oil which is also known as petrolatum liquid, is a mixture of liquid hydrocarbons obtained from petroleum. See The Merck Index, Tenth Edition, Entry 7048, p. 1033 (1983) and International Cosmetic Ingredient Dictionary, Fifth Edition, vol. 1, p.415-417 (1993), which are incorporated by reference herein in their entirety.

(ii) Petrolatum: Petrolatum which is also known as petroleum jelly, is a colloidal system of nonstraight-chain solid hydrocarbons and high-boiling liquid hydrocarbons, in which most of the liquid hydrocarbons are held inside the micelles. See The Merck Index, Tenth Edition, Entry 7047, p. 1033 (1983); Schindler, Drug. Cosmet. Ind., 89, 36-37, 76, 78-80, 82 (1961); and International Cosmetic Ingredient Dictionary, Fifth Edition, vol. 1, p. 537 (1993), which are incorporated by reference herein in their entirety.

(iii) Straight and branched chain hydrocarbons having from about 7 to about 40 carbon atoms: These materials include dodecane, isododecane, squalane, cholesterol, hydrogenated polyisobutylene, docosane (i.e., a C<sub>22</sub> hydrocarbon), hexadecane, isohexadecane (a commercially available hydrocarbon sold as Permethyl® 101A by Presperse, South Plainfield, NJ). Also useful are the C<sub>7-40</sub> isoparaffins, which are C<sub>7-40</sub> branched hydrocarbons.

(iv) C<sub>1-30</sub> alcohol esters of C<sub>1-30</sub> carboxylic acids and of C<sub>2-30</sub> dicarboxylic acids: including straight and branched chain materials as well as aromatic derivatives (as used herein in reference to the hydrophobic component, mono- and poly- carboxylic acids include straight chain, branched chain and aryl carboxylic acids). Nonlimiting examples include diisopropyl sebacate, diisopropyl adipate, isopropyl myristate, isopropyl palmitate, methyl palmitate, myristyl propionate, 2-ethylhexyl palmitate, isodecyl neopentanoate, di-2-ethylhexyl

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maleate, cetyl palmitate, myristyl myristate, stearyl stearate, isopropyl stearate, methyl stearate, cetyl stearate, behenyl behenate, dioctyl maleate, dioctyl sebacate, diisopropyl adipate, cetyl octanoate, diisopropyl dilinoleate.

(v) Mono-, di- and tri- glycerides of C<sub>1-30</sub> carboxylic acids: For example, caprylic/capric triglyceride, PEG-6 caprylic/capric triglyceride, PEG-8 caprylic/capric triglyceride.

(vi) Alkylene glycol esters of  $C_{1-C30}$  carboxylic acids: For example, ethylene glycol mono- and di- esters, and propylene glycol mono- and di- esters of  $C_{1-30}$  carboxylic acids e.g., ethylene glycol distearate.

(vii) C<sub>1-30</sub> mono- and poly- esters of sugars and related materials: These esters are derived from a sugar or polyol moiety and one or more carboxylic acid moieties. Depending on the constituent acid and sugar, these esters can be in either liquid or solid form at room temperature. The ester materials are further described in, US Patent No. 2,831,854, 4,005,196, and 4,005,195, Jandacek, issued January 25, 1977; US Patent No. 5,306,516 and 5,306,515, Letton et al., issued April 26, 1994; US Patent No. 5,305,514, Letton et al., issued April 26, 1994; US Patent No. 4,797,300, Jandacek et al., issued January 10, 1989; US Patent No. 3,963,699, Rizzi et al, issued June 15, 1976; US Patent No. 4,518,772, Volpenhein, issued May 21, 1985; and US Patent No. 4,517,360, Volpenhein, issued May 21, 1985.

(viii) Vegetable oils and hydrogenated vegetable oils: Examples of vegetable oils and hydrogenated vegetable oils include safflower oil, castor oil, coconut oil, cottonseed oil, menhaden oil, palm kernel oil, palm oil, peanut oil, soybean oil, rapeseed oil, linseed oil, rice bran oil, pine oil, sesame oil, sunflower seed oil, hydrogenated safflower oil, hydrogenated castor oil, hydrogenated coconut oil, hydrogenated cottonseed oil, hydrogenated menhaden oil, hydrogenated palm kernel oil, hydrogenated palm oil, hydrogenated peanut oil, hydrogenated soybean oil, hydrogenated rapeseed oil, hydrogenated linseed oil, hydrogenated rice bran oil, hydrogenated sesame oil, hydrogenated sunflower seed oil, and mixtures thereof.

(ix) Animal fats and oils: These oils include lanolin and derivatives thereof, and cod liver oil.

(x) Other materials: Also useful are  $C_{\underline{4-20}}$  alkyl ethers of polypropylene glycols,  $C_{\underline{1-20}}$  carboxylic acid esters of polypropylene glycols, and di- $C_{\underline{8-30}}$  alkyl ethers.

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### E. Cosmetically-Acceptable Carrier

The transparent compositions of the present invention contain a cosmetically-acceptable carrier. The carrier can include a polyhydric alcohol and/or water solvent; preferably water. The composition contains from about 60% to about 99.8% of the carrier, preferably from about 80% to about 99.5%.

In one embodiment, the carrier includes water and lower alkyl alcohols. Lower alkyl alcohols useful herein are  $C_{\underline{1-6}}$  alkyl monohydric alcohols; preferably  $C_{\underline{2-3}}$  alkyl alcohols. Preferred lower alkyl alcohols include ethyl alcohol, isopropyl alcohol, and mixtures thereof.

Preferred polyhydric alcohols useful herein include, but are not limited to, polyalkylene glycols, more preferably alkylene polyols and their derivatives including glycerin, propylene glycol, dipropylene glycol, tripropylene glycol, polyethylene glycol and derivatives thereof, sorbitol, hydroxypropyl sorbitol, erythritol, threitol, pentaerythritol, xylitol, glucitol, mannitol, hexylene glycol, 1,3-butylene glycol, 1,2,6-hexanetriol, glycerol, ethoxylated glycerol, propoxylated glycerol, soluble collagen, gelatin, and mixtures thereof. Preferred moisturizing agents are glycerin, 1,3-butylene glycol, glucose, trimethylglycine, urea, or mixtures thereof; more preferably glycerin or 1,3-butylene glycol.

### F. Optional Components

The transparent composition of the present invention may further comprises optional components. Herein, "optional components" means one or more compatible solid or liquid fillers, diluents, extenders and the like, which are commonly used in cosmetics as defined herein. The term "compatible" herein means that the components of the compositions of this invention are capable of being commingled with each other, in a manner such that there is no interaction which would substantially reduce the efficacy of the composition under ordinary use situations.

The optional components useful herein include an active and inactive components. The type of the optional components utilized in the present invention depend on the type of product desired and may comprise several types of carriers including, but not limited to, oil-in-water or water-in-oil emulsions.

### 1) Actives

The optional components useful herein may comprise active components. Examples of such actives include, but are not limited to, a vitamin B<sub>3</sub> compound, anti-oxidants and radical scavengers, anti-inflammatory agents, antimicrobial

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agents, sunscreens and sunblocks, and chelators. Other actives useful herein include vitamin A (e.g., retinoid which is commercially available from a number of sources, for example, Sigma Chemical Company (St. Louis, MO), and Boerhinger Mannheim (Indianapolis, IN) and described in US Patent 4,677,120, Parish et al., issued June 30, 1987; US Patent 4,885,311, Parish et al., issued December 5, 1989; US Patent 5,049,584, Purcell et al., issued September 17, 1991; US Patent 5,124,356, Purcell et al., issued June 23, 1992; and Reissue Patent 34,075, Purcell et al., issued September 22, 1992); and vitamin K.

(i) Vitamin B<sub>3</sub> Compounds: Vitamin B<sub>3</sub> compounds enhance skin appearance by improving skin condition, including treating signs of skin aging, more especially wrinkles, lines, and pores. Vitamin B<sub>3</sub> compounds are preferably present from about 0.01% to about 50%, more preferably from about 0.1% to about 10%, even more preferably from about 0.5% to about 10%, and still more preferably from about 1% to about 5%.

Herein, "vitamin B<sub>3</sub> compound" means a compound having the formula:



wherein R is -CONH<sub>2</sub> (e.g., niacinamide), -CH<sub>2</sub>OH (e.g., nicotinyl alcohol); and derivatives thereof.

Exemplary derivatives of the foregoing vitamin B<sub>3</sub> compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids, nicotinic acid N-oxide and niacinamide N-oxide.

Suitable esters of nicotinic acid include nicotinic acid esters of from 1 to about 22 carbons, preferably 1 to about 16 carbons, more preferably alcohols from about 1 to about 6 carbons. The alcohols are suitably straight-chain or branched chain, cyclic or acyclic, saturated or unsaturated (including aromatic), and substituted or unsubstituted. The esters are preferably non-vasodilating. As used herein, "non-vasodilating" means that the ester does not commonly yield a visible flushing response after application to the skin in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds may cause vasodilation not visible to the naked eye, *i.e.*, the ester is non-rubifacient). Non-vasodilating esters of nicotinic

acid include tocopherol nicotinate and inositol hexanicotinate; tocopherol nicotinate is preferred.

Other derivatives of the vitamin B<sub>3</sub> compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of derivatives of niacinamide useful herein include nicotinyl amino acids, derived, for example, from the reaction of an activated nicotinic acid compound (e.g., nicotinic acid azide or nicotinyl chloride) with an amino acid, and nicotinyl alcohol esters of organic carboxylic acids (e.g., C<sub>1-18</sub>). Specific examples of such derivatives include nicotinuric acid (C<sub>8</sub>H<sub>8</sub>N<sub>2</sub>O<sub>3</sub>) and nicotinyl hydroxamic acid (C<sub>6</sub>H<sub>6</sub>N<sub>2</sub>O<sub>2</sub>), which have the following chemical structures:

nicotinuric acid:

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15 nicotinyl hydroxamic acid:

Exemplary nicotinyl alcohol esters include nicotinyl alcohol esters of the carboxylic acids salicylic acid, acetic acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of vitamin B<sub>3</sub> compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methylnicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid, methyl isonicotinic acid, thionicotinamide, nialamide, 1-(3-pyridylmethyl) urea, 2-mercaptonicotinic acid, nicomol, and niaprazine.

Nonlimiting examples of the above vitamin B<sub>3</sub> compounds are well known in the art and are commercially available from a number of sources, *e.g.*, the Sigma Chemical Company (St. Louis, MO); ICN Biomedicals, Inc. (Irvin, CA) and Aldrich Chemical Company (Milwaukee, W!).

WO 00/61098 PCT/US99/08232

12

One or more vitamin B<sub>3</sub> compounds may be used herein. Preferred vitamin B<sub>3</sub> compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

When used, salts, derivatives, and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating skin condition described herein.

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Salts of the vitamin B<sub>3</sub> compound are also useful herein. Nonlimiting examples of salts of the vitamin B<sub>3</sub> compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide, carbonate, preferably chloride), and organic carboxylic acid salts (including mono-, di- and tri- C<sub>1-18</sub> carboxylic acid salts, e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the vitamin B<sub>3</sub> compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic and D-losascorbic Acid with Nicotinic Acid and Its Amide", J. Organic Chemistry, Vol. 14, 22-26 (1949). Wenner describes the synthesis of the ascorbic acid salt of niacinamide.

In a preferred embodiment, the ring nitrogen of the vitamin B<sub>3</sub> compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the skin becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the vitamin B<sub>3</sub> compound is essentially uncomplexed. Therefore, if the composition contains the vitamin B<sub>3</sub> compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the skin. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility can be readily determined by one having ordinary skill in the art.

More preferably the vitamin B<sub>3</sub> compound is substantially uncomplexed in the composition prior to delivery to the skin. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the vitamin B<sub>3</sub> compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the vitamin B<sub>3</sub> compound and materials

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which complex therewith are in different phases. Such approaches are well within the level of ordinary skill in the art.

Thus, in a preferred embodiment, the vitamin B<sub>3</sub> compound contains a limited amount of the salt form and is more preferably substantially free of salts of a vitamin B<sub>3</sub> compound. Preferably the vitamin B<sub>3</sub> compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The vitamin B<sub>3</sub> compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about 50% of the salt.

The vitamin B<sub>3</sub> compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The vitamin B<sub>3</sub> compound is preferably substantially pure, more preferably essentially pure.

(ii) Anti-Oxidants and Radical Scavengers: Anti-oxidants and radical scavengers are especially useful for providing protection against UV radiation which can cause increased scaling or texture changes in the stratum comeum and against other environmental agents which can cause skin damage.

Anti-oxidants and radical scavengers such as tocopherol (vitamin E), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, propyl gallate, alkyl esters of uric acid, amines (*i.e.*, N,N-diethylhydroxylamine, aminoguanidine), sulfhydryl compounds (*i.e.*, glutathione), lycine pidolate, arginine pilolate, bioflavonoids, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape skin/seed extracts, melanin, and rosemary extracts may be used. Preferred anti-oxidants/radical scavengers are selected from tocopherol sorbate and other esters of tocopherol, more preferably tocopherol sorbate. For example, the use of tocopherol sorbate in topical compositions and applicable to the present invention is described in U.S. Patent 4,847,071, Bissett et al, issued July 11, 1989.

(iii) Anti-Inflammatory Agents: Anti-inflammatory agents enhance the skin appearance benefits, by for example, contribution of uniformity and acceptable skin tone and/or color.

Preferably, the anti-inflammatory agent includes a steroidal anti-inflammatory agent and an non-steroidal anti-inflammatory agent. Preferred steroidal anti-inflammatory for use is hydrocortisone.

The variety of compounds encompassed by this group are well-known to those skilled in the art. For detailed disclosure of the chemical structure,

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synthesis, side effects, etc. of non-steroidal anti-inflammatory agents, reference may be had to standard texts, including Anti-inflammatory and Anti-Rheumatic Drugs, K. D. Rainsford, Vol. I-III, CRC Press, Boca Raton, (1985), and Anti-inflammatory Agents, Chemistry and Pharmacology, 1, R. A. Scherrer, et al., Academic Press, New York (1974), each incorporated herein by reference.

So-called "natural" anti-inflammatory agents are also useful. Such agents may suitably be obtained as an extract by suitable physical and/or chemical isolation from natural sources (i.e., plants, fungi, by-products of microorganisms). For example, alpha bisabolol, aloe vera, Manjistha (extracted from plants in the genus Rubia, particularly Rubia Cordifolia), and Guggal (extracted from plants in the genus Commiphora, particularly Commiphora Mukul), kola extract, chamomile, and sea whip extract, may be used.

(iv) Antimicrobial Agent: As used, "antimicrobial agents" means a compound capable of destroying microbes, preventing the development of microbes or preventing the pathogenic action of microbes. Antimicrobal agents are useful, for example, in controlling acne. Preferred antimicrobial agents useful in the present invention are benzoyl peroxide, erythromycin, tetracycline, clindamycin, azelaic acid, sulfur resorcinol phenoxyethanol, and Irgasan™ DP 300 (Ciba Geigy Corp., U.S.A.). A safe and effective amount of an antimicrobial agent may be added to compositions of the present invention, preferably from about 0.001% to about 10%, more preferably from about 0.01% to about 5%, still more preferably from about 0.05% to about 2%.

(v) Sunscreens and Sunblocks: Sunscreens and sunblocks generally prevent excessive scaling and texture changes of the stratum corneum by exposure of ultraviolet light and may be added to the composition of the present invention. Suitable sunscreens and sunblocks may be organic.

A wide variety of conventional sunscreens and sunblocks are suitable for use herein. See, U.S. Patent 5,087,445, Haffey et al, issued February 11, 1992; U.S. Patent 5,073,372 and 5,073,371, Turner et al, issued December 17, 1991; and Segarin, et al, at Chapter VIII, pages 189 et seq., of Cosmetics Science and Technology (1972), which discloses numerous suitable sunscreens and sunblocks. Preferred among those sunscreens and sunblocks which are useful in the compositions are those selected from 2-ethylhexyl-p-methoxycinnamate (commercially available as PARSOL MCX), butylmethoxydibenzoyl-methane, 2-hydroxy-4-methoxybenzo-phenone, octocrylene, oxybenzone, homomenthyl

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salicylate, octyl salicylate, 4,4'-methoxy-t-butyldibenzoylmethane, 4-isopropyl dibenzoylmethane, 3-benzylidene camphor, 3-(4-methylbenzylidene) camphor, Eusolex™ 6300, Octocrylene, Parsol 1789, and mixtures thereof.

Also particularly useful in the compositions are sunscreens and sunblocks such as those disclosed in U.S. Patent 4,937,370, Sabatelli, issued June 26, 1990, and U.S. Patent 4,999,186, Sabatelli, issued March 12, 1991. The sunscreens and sunblocks disclosed therein have, in a single molecular, two distinct chromophore moieties which exhibit different ultraviolet radiation absorption spectra. One of the chromophore moieties absorbs predominantly in the UVB radiation range and the other absorbs strongly in the UVA radiation range. These sunscreens and sunblocks provide higher efficacy, broader UV absorption, lower skin penetration and longer lasting efficacy relative to conventional sunscreens and sunblocks.

Exact amounts will vary depending upon the sunscreen chosen and the desired Sun Protection Factor (SPF). SPF is a commonly used measure of photoprotection of a sunscreen against erythema. See Federal Register, Vol. 43, No. 166, pp. 38206-38269, August 25, 1978.

(vi) Chelators: As used herein, "chelator" refers to a compound that reacts for removing a metal ion from a system by forming a complex so that the metal ion cannot readily participate in or catalyze chemical reactions. The inclusion of a chelator is especially useful for providing protection against UV radiation which can contribute to excessive scaling or skin texture changes and against other environmental agents which can cause skin damage.

Exemplary chelators that are useful herein are disclosed in U.S. Patent 5,487,884, Bissett et al, issued January 30, 1996; PCT application 91/16035 and 91/16034, Bush et al, published October 31, 1995. Preferred chelators are furildioxime and derivatives thereof.

### 2) Inactive Ingredients

In addition to the above described components, the composition of the present invention may further include preservatives and preservative enhancers such as water-soluble or solubilizable preservatives including Germall 115, methyl, ethyl, propyl and butyl esters of hydroxybenzoic acid, benzyl alcohol, EDTA, Bronopol (2-bromo-2-nitropropane-1,3-diol), phenoxyethanpl, and phenoxypropanol; antifoaming agents; binders; biological additives; bulking

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agents; coloring agents; perfumes, essential oils, and solubilizers thereof; natural extracts; compounds which stimulate collagen production.

### G. Method for Making Composition

The compositions of the present invention are generally prepared by any method conventionally used for providing skin care compositions, particularly for skin lotions, that are known in the art. Such methods typically involve mixing of the ingredients in one or more steps to a relatively uniform state, with or without heating, cooling, and the like. Typical methods are described in, for example are described in Harry's Cosmeticology, 7th Ed., Harry & Wilkinson (Hill Publishers, London 1982).

#### **EXAMPLES**

The following examples further describe and demonstrate embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention. Where applicable, ingredients are identified by chemical or INCI name, or otherwise defined below.

### Examples 1-3

Examples 1 - 3 of the transparent composition are prepared from the following ingredients by the formulating techniques set forth below.

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Example		1	. 2	3
		lotion	essence	gel
phase A	hydrogenated lecithin	0.2	1.4	0.3
	caprylic/capric triglyceride	0.4	4.0	0.8
	squalane	0.4	4.0	0.8
	polysorbate 60	0.2	1.5	0.4
	sucrose palmitate	0.05	0.6	0.15
	sucrose distearate	0.2	1.4	0.3
phase B	1,3-butylene glycol	2.0	15.0	5.0
	paraben	0.1	0.2	0.1
phase C	de-ionized water	20.0	60.0	60.0
phase D	hydroxyethylcellulose	0.04	-	_ •
	cetyl hydroxyethylcellulose	-	0.2	1.0
	pullulane	_	-	0.1
	locust bean gum	0.3	0.1	0.1
	glycerin	2.0	2.0	4.0
	phenoxyethanol	0.2	0.2	0.2
	de-ionized water	up to	100	

The compositions above described are suitably made as follows:

- 1 Mix phase A ingredients using propeller type and a suitably size vessel mixer and heat to about 70-75°C.
- Add phase B ingredients to phase A mixture and mix at about 70-75°C.
- Add phase C into mixture of phase A-B at about 70-75°C.
- 4 After cooling of the phase A-C mixture, add mixture of phase D.

The embodiments disclosed and represented by the previous examples have many advantages. For example, the oil-in-water transparent composition comprising lecithin, water-soluble nonionic polymer, and oily component herein provide improved transparency and spreadability of products and good skin feel such as moisturizing the skin without greasy feeling to skin.

It is understood that the foregoing detailed description of examples and embodiments of the present invention are given merely by way of illustration, and that numerous modifications and variations may become apparent to those WO 00/61098 PCT/US99/08232

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skilled in the art without departing from the spirit and scope of the invention; and such apparent modifications and variations are to be included in the scope of the appended claims.

### What is claimed is:

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- 1. A transparent composition comprising a phospholipid, a water-soluble nonionic polymer, an oily component, and a cosmetic acceptable carrier, wherein the concentration of the water-soluble nonionic polymer is less than 2.0 wt% by weight of the composition.
- 2. The transparent composition of Claim 1, wherein the concentration of the water-soluble nonionic polymer is from about 0.02 to about 1.0 wt%.
- 3. The transparent composition of Claim 2, wherein the viscosity of the transparent composition is from about 2 to about 10,000 cps.
- 4. The transparent composition of Claim 3, wherein the viscosity of the transparent composition is from about 2 to about 500 cps.
- 5. The transparent composition of Claim 4, wherein the viscosity of the transparent composition is from about 4 to about 200 cps.
- 6. The transparent skin care composition of Claim 1, wherein the composition comprises two or more oily components.
- 7. The transparent skin care composition of Claim 6, wherein the water-soluble nonionic polymer is selected from the group consisting of hydroxyethylcellulose, cetyl hydroxyethylcellulose, locust bean gum, pullulan, sclerotium gum, termarind seed gum, and polyvinylalcohol, polyvinylpyrorridon.
- 8. A transparent skin care composition comprising:
  - (a) from about 0.05 to about 5.0 wt% of a phospholipid;
  - (b) from about 0.01 to about 2.0 wt% of a water-soluble nonionic polymer; and
- (c) from about 0.05 to about 15.0 wt% of an oily component; wherein the viscosity of the transparent composition is from about 2 to about 10,000 cps.

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A. CLASSI IPC 7	FICATION OF SUBJECT MATTER A61K7/48 A61K7/00	-	
	o International Patent Classification (IPC) or to both national classific SEARCHED	cation and IPC	
	SEARCHED  ocumentation searched (classification system followed by classification	ion symbols)	
IPC 7	A61K		
Documenta	tion searched other than minimum documentation to the extent that s	such documents are included in the fields so	earched
Electronic d	lata base consulted during the international search (name of data ba	ase and, where practical, search terms used	1)
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the rel	levant passages	Relevant to claim No.
		•	
X	WO 93 18752 A (PHARMOS CORP)		1,2,8
A	30 September 1993 (1993-09-30) page 1, line 4 - line 9		7
	page 3, line 7 -page 4, line 1		
:	page 6, line 22 - line 34 page 7, line 13 - line 17		
	page 8, line 10 -page 9, line 16		
	page 10, line 28 -page 11, line 7	7	
	page 13, line 26 - line 32 examples 1,15,16		
Х	DE 44 04 085 A (RHONE POULENC ROP	RER GMBH)	1,6-8
	10 August 1995 (1995-08-10)	·	
	page 2, line 19 - line 22   page 2, line 55 - line 58		
	examples 1,3		
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	her documents are listed in the continuation of box C.	X Patent family members are listed	in annex.
		"I later document published after the inte or priority date and not in conflict with	mational filing date the application but
consid	ent defining the general state of the art which is not lered to be of particular relevance	cited to understand the principle or the invention	eory underlying the
filing d	1210	"X" document of particular relevance; the c cannot be considered novel or cannot	be considered to
which	int which may throw doubts on priority claim(s) or is cited to establish the publication date of another n or other special reason (as specified)	involve an inventive step when the do "Y" document of particular relevance; the c	laimed invention
"O" docume	means to an oral disclosure, use, exhibition or	cannot be considered to involve an inv document is combined with one or mo ments, such combination being obviou	re other such docu-
"P" docume	ent published prior to the international filing date but	in the art. "&" document member of the same patent	•
Date of the	actual completion of the international search	Date of mailing of the international sea	ırch report
2	3 December 1999	11/01/2000	
Name and n	nailing address of the ISA	Authorized officer	
	European Patent Office, P.B. 5818 Patentiaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo ni,	04-1 5	
	Fax: (+31-70) 340-3016	Cielen, E	

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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Week 199239 Derwent Publications Ltd., London, GB; AN 1992-320239 XP002126642 YOKOTA TAKASHI ET AL.: "LIQUID CRYSTAL COMPOSITIONS AND COSMETIC CONTAINING THE SAME" & JP 04 224886 A (KOSE KK), 14 August 1992 (1992-08-14) abstract	1,2,6-8
A	abstract  DE 196 18 809 C (GOLDWELL GMBH) 11 December 1997 (1997-12-11) abstract page 2, line 41 - line 47 page 3, line 16 - line 36 example 1	1,2,6-8

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Imamational application No.

PCT/US 99/08232

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.:     because they relate to subject matter not required to be searched by this Authority, namely:
2. X Claims Nos.: 3-5 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  SEE FURTHER INFORMATION sheet PCT/ISA/210
Claims Nos.:     because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box il Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)
This International Searching Authority found multiple inventions in this International application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 3-5

Present claims 3-5,8 relate to a composition defined by reference to the parameter "viscosity". The use of this parameter in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is not fully possible to compare the parameter the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, the search has been restricted to compositions comprising the compounds as described in claims 1,2,7 and 8 (compounds (a)-(c)), obvious variants thereof and the general idea underlying the application.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

information on patent family members

Inter. nai Application No PCT/US 99/08232

Patent document cited in search report		Publication date	Patent family member(s)		Publication date	
WO 9318752	A	30-09-1993	AU CA EP JP ZA	3935293 A 2132736 A 0671903 A 7505368 T 9302170 A	21-10-1993 30-09-1993 20-09-1995 15-06-1995 28-10-1993	
DE 4404085	A	10-08-1995	NONE			
JP 4224886	Α	14-08-1992	JP	2929318 B	03-08-1999	
DE 19618809	С	11-12-1997	NONE			